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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
CANELLA, KAREN A

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/814,661	ROTHSTEIN ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 24-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *14-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Acknowledgment is made of applicants election with traverse of Group IV, Claims 14-23, drawn to a screening assay for identifying compounds which reduce the division rate of a cell by altering the interaction between ribonucleotide reductase and the SmL1 protein. The traversal is on the ground that the examiner must examine the entire application on the merits , even though it includes claims to distinct inventions , if the search and examination can be made without serious burden. Applicant argues that there would be no serious burden on the examiner because a search of the prior art relevant to Groups I, II, II and V would not be a serious burden once the prior art for Group IV has been identified. This has been considered but not found persuasive. The claims of Groups I, II, III and V are classified differently from each other and from the invention of Group IV, necessitating different searches in the U.S. Patent shoes. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made FINAL.

2. Claims 1-36 are pending. Claims 1-13 and 24-36, drawn to non-elected inventions, are withdrawn from consideration. Claims 14-23 are examined on the merits.

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 26, line 29. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 14-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention..

Claims 14-23 are rendered vague and indefinite in the recitation of "SML1" as the only means of identifying the protein upon which the claim method depends. The use of a laboratory designation only to identify a protein renders the claim indefinite as other laboratories can use different designation to identify the same protein and vice versa. For example, the human spasmolytic protein is identified as SML1 (The abstract of Theisinger et al, Human Genetics, 1992, Vol. 89, pp. 681-682). Further, the application has not set forth a definition of an Sml-1 protein which could be used to determine the metes and bounds of what constitutes a Sml1 protein. Amendment of the claim to recite a sequence identifier or a deposit accession number would overcome this rejection.

Claims 20-23 are vague and indefinite in the recitation of "previously unknown". It is unclear what the reference point is for "previous". For purpose of examination, it will be considered as "of the priority date sought".

The term "small" in claim 15 is a relative term which renders the claim indefinite. The term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. .

Claim 16 is vague and indefinite in the recitation or "a variant of a Sml1 protein". The specification fails to provide a definition for a Sml1 variant that would define the metes and bounds of the claim.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 14-23 are method claims dependent on the identity of the SML1 protein. The specification states on page 10, lines 29-35 that an embodiment of a SMl1 protein is exemplified by SEQ ID NO:2. The polynucleotide encoding SEQ ID NO:2 was identified as an allele of the S ceriviseae Mec-1 gene which can rescue the lethality of mutant Mec-1. The specification further contemplates that homologues of Sml1, such as a human, microbial plant of insect Sml1 are other embodiments of Sml1. The specification fails to provide a written description of said homologs and further states that there are no known homologs of Sml1 (Zhao et al, Molecular Cell, 1998, vol. 2, pp. 329-340, page 330, second column, lines 9-11). The specification states that it is likely that a homolog of Sml1 will be identified in human as the subunits of ribonucleotide reductase in yeast are closely related to those of humans (page 26, lines 33-36). This is not a persuasive argument because mammalian cells have two pathways of dNTP synthesis in contrast to yeast which has a single pathway (Zhao et al, ibid, page 336, second column, second full paragraph). Thus, the conservation of a Sml1 protein in mammalian cells would not be indicated as there is divergence of the pathways controlling dNTP synthesis between yeast and mammalian cells. Thus, the claims are dependent upon a genus of proteins which include unknown structural attributes. The general knowledge and skill in the art does not supplement the deficiencies of the disclosure because specific, not general guidance is what is needed. The disclosure of SEQ ID NO:2 does not anticipate this genus, because numerous structural attributes are contained within the genus. The specification does not teach what structural attributes are necessary within the homologues of SEQ ID NO:2, thus the common attributes of the genus are not described. Further, it is noted that the Sml1 protein is encoded by an allele of mec-1. The nature of alleles is that they are variant structures, and the structure of one allele does not provide information about the structure of another. One of skill in the art would conclude that applicant failed to disclose a representative number of species within the claimed genus, therefore, applicant was not I possession of the claimed genus of Sml1 proteins.

Claims 20-23 comprise the specific embodiment of "a previously unknown compound". Claims 20-23 are drawn to a genus of compounds which are identified by the assay of claim 14, and were "previously unknown". It is noted above that claims 20-23 are vague and indefinite without a reference point for "previous". The specification has failed to provide an adequate written description of a single "previously unknown" compound" which was identified in the specification by means of the assay of claim 14. One of skill in the art would conclude that

applicant failed to provide a representative number of species which would anticipate the claimed genus. Thus, applicant was not in possession of the genus of "previously unknown" compounds.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Nasr et al (C R Acad Sci III, 1994, Vol. 317, pp. 607-613) as evidenced by Sanchez et al (Science, 1996, Vol. 271, pp. 357-360).

Claims 14 , 15 and 18 are drawn to a screening assay for identifying compounds that are capable of reducing the division rate of a cell by altering an interaction between a ribonucleotide reductase and a Sml1 protein in the cell, which comprises: (a) contacting the cell with a compound, (b) comparing the division rate of the cell in step (a) with the division rate of the cell in the absence of the compound so as to determine whether the compound alters the interaction between the ribonucleotide reductase and the Sml1 protein of the cell, thereby reducing the cell division rate of the cell. Claim 15 embodies the assay of claim 14 wherein the compound is an organic compound, a peptide, an inorganic compound, a lipid, a peptidomimetic or a small synthetic compound. Claim 18 embodies the screening assay of claim 14, wherein the cell is a yeast cell, a mammalian cell, a plant cell, an insect cell or a microbe.

Nasr et al disclose an antisense molecule to an allele of the yeast YBR1012 gene. Sanchez et al disclose MEC1 as YBR1022. It appears that the allele of MEC1 disclosed by Nasr et al is the same as the instant Sml1 because Sml1 is an allele of MEC1. The antisense

allele disclosed by Nasr et al would decrease the amount of Sml1 and alter the interaction between Sml1 and ribonucleotide reductase in the cell, as the resulting decrease in Sml1 levels would result in a decrease of Sml1 bound to ribonucleotide reductase.

8. Claims 14-16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Sanchez et al (Science, 1996, Vol. 271, pp. 357-360). The specific embodiments of claims 14, 15 and 18 are set forth above. Claim 16 embodies the screening assay of claim 15, wherein the peptide or the peptidomimetic is a variant of a Sml1 protein or a fragment thereof. Sanchez et al disclose that introduction of a single copy of MEC1 into a mec1 mutant dependent on overproduction of RAD53 relieves the dependency on RAD53 overproduction (page 357, Figure 1 (B)). It is noted that claim 16 is vague and indefinite as to the metes and bounds of a "variant of a Sml1 protein". The Mec1 protein expressed as the result of the introduction of the gene encoding MEC1 is a variant of Sml1 because Sml1 is defined as a allele of Mec1.

9. Claims 14, 15, 18 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Li et al (U.S. 5,767,134). The specific embodiments of claims 14, 15 and 18 are set forth above. Claim 19 embodies the assay of claim 14 wherein the mammalian cell is a human cell, a hamster cell, a mouse cell, a rat cell or a monkey cell.

Li et al disclose a method of decreasing the activity of ribonucleotide reductase in a human cell comprising the administration of 3-aminopyridine-2-carboxyaldehyde thiosemicarbazone or 3-amino-4-methylpyridine-2-carboxaldehyde thiosemicarbazone (column 1, lines 15-50 and column 2, lines 31-34 and column 4, lines 35-41). The compounds disclosed by Li et al inhibit the activity of ribonucleotide reductase. The reference does not specifically teach that the inhibition of the ribonucleotide reductase alters the interaction between said ribonucleotide reductase and Sml1, however, the administration of the compounds disclosed by Li et al result in inhibition of ribonucleotide reductase and a reduction in tumor growth which appears to have the same effect as the claimed alteration of the interaction between ribonucleotide reductase and Sml1 which reduces the rate of cell division. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of a compound which alters the interaction between ribonucleotide reductase and

Sml1 resulting in a decrease in cell division rate. . In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

10. Claims 14, 15, 18 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Cooperman et al (U.S. 6,030,942). The specific embodiments are recited above. Cooperman et al disclose an assay for the identification of ribonuclease reductase peptidomimetic that are able to reduce the division rate of the cell (column 12, lines 55-58). Cooperman et al disclose that it is desirable to inhibit the ribonuclease reductase of a pathological cell type of a human, such as a cancer cell (column 14, lines 17-19), thus fulfilling the specific embodiments of claims 18 and 19 drawn to mammalian cells and human cells, respectively. Cooperman et al do not specifically disclose that the peptidomimetic will alter the interaction between the ribonucleotide reductase and the Sml1 protein in the cell, however, this would be inherent in the method of Cooperman et al as the peptidomimetics would compete with ribonucleotide reductase for binding to Sml1.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella

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7/28/03